REMARKS/ARGUMENTS

Support for the amended claim is found at the originally filed claims and throughout the originally filed specification.

No new matter is believed to have been added.

The 35 U.S.C. Section 101 rejection of Claims 39-46 as lacking patentable utility is respectfully traversed. Applicants have submitted, along with this paper, Declarations under 37 C.F.R. Section 1.132 by Dr. Alain Favier and and Dr. Michel Seve. Dr.'s Favier and Seve are inventors in the present application.

Present Claim 39 is drawn to "A method detecting Type 1 diabetes by detecting the presence of auto antibodies specifically targeting the beta cells of the pancreatic islets of Langerhans..."

At the outset, the Office, at page 6 of the Official Action, asserts "the specification discloses nothing about the autoantibodies of the claimed method, indeed, the word "autoantibody" does not even appear in the present specification."

The Office is wrong.

At originally filed Claim 29, that is part of the originally filed specification, the term "auto antibodies" is described (e.g., "the search for auto antibodies directed against said protein.").

Paragraph 104 of the originally filed specification, describes, in part "...the search for auto-antibodies directed against the protein according to the invention."

Accordingly, the term "auto antibodies" is found in the originally filed specification and is thus properly included in present Claim 39.

Having established that "auto antibodies" is described in the originally filed specification, Applicants now address the assertion, at page 5 of the Official Action, that "The claimed method is not supported by a substantial asserted utility because neither the

claims nor the specification disclose any reason for the detection of autoantibodies to the proteins of SEQ ID NOS: 2 or 7-10 (ZnT-8 and fragments thereof)."

MPEP 2107.02 VI describes, in part, that "After evidence or argument is submitted by the Applicant in response [to a lack of utility rejection], patentability is determined by the totality of the record, by a preponderance of the evidence with due consideration to persuasiveness of the argument." "An Applicant can do this using any combination of the following: amendments to the claims, arguments or reasoning, or new evidence submitted in an affidavit or declaration under 37 C.F.R. 1.132, or in a printed publication."

Applicants note that the standard is "preponderance of the evidence" and that "preponderance of the evidence" is a lower burden to meet than those burdens required for both "beyond a reasonable doubt" and "clear and convincing evidence." Accordingly, Applicants only need meet the relatively low "preponderance of the evidence" standard, and as described in MPEP 2107.02 VI, may do so by amending the claims, by arguments or reason, by addidavits, and by printed publications. Applicants, in this paper, employ all of these tools.

The effective filing date of the present application is November 18, 2003, the filing date of priority application PCT/FR03/03413.

Accordingly, publications with publication dates on or before November 18, 2003, tend to establish what was known in the field of the invention on or before the present Application's filing date.

As described in the Favier Declaration, under numbered heading 4, the originally filed specification, at page 6, lines 24-27, describes that the protein ZnT-8 is specifically expressed in the beta cells of the pancreatic islets of Langerhans.

As described above, in at least two places, the term "auto antibodies" is employed in the originally filed specification.

In the Favier Declaration, under numbered heading 5, Dr. Favier cites Cell 85:291-297 (1996) (herein after "Cell"). For the Office's convenience, Applicants have enclosed a copy of this publication along with this paper. Applicants note that the year of publication, 1996, is before the November 18, 2003, effective filing date of the present application.

Dr. Favier, under numbered heading 5, describes, citing Cell, that "Type 1 diabetes is an autoimmune disease resulting from specific destruction of the insulin-producing beta cells of the Langerhans islets of the pancreas." Dr. Favier further states: "It has been demonstrated that the physiological destruction of beta cells is a crucial event at disease outset, initiating autoimmunity against these cells (citing Nature 414:792-798 (2001), herein after "Nature": the Nature publication is before present application's effective filing date of November 18, 2003; a copy of the publication is enclosed with this paper for the Office's convenience).

As discussed under numbered heating 6 of the Favier Declaration, Kukreja and Mcclarin review "what was known in 1999 about type 1 diabetes, also called immune-mediated diabetes (IMD)." "At the time of clinical diagnosis of IMD, about 80% of the beta cells have been destroyed, but autoantibodies to beta cells are detectable long before a person develops diabetes." "It appears that the nature, intensity, and antigenic spreading of the reactivity of these autoantibodies distinguish individuals who develop diabetes from those who do not" (Journal of Clinical Endrocrinology and Metabolism – publication date 1999; this publication has a publication date before the effective filing date of the present application).

Citing Batstra et al., Clinical Laboratory 2001, published before the effective Filing Date of the Application, a copy of which is enclosed with this paper for the Office's convenience, the Favier Declaration further describes "Bastra et al., also mention that discrimination between type 1 and type 2 diabetes is important for determining the most appropriate treatment, and that this can be performed by detecting autoantibodies targeting beta cells of the islets of Langerhans."

Under numbered heading 7, the Favier Declaration, citing Diabetes 50:1749-54 (2001), (herein after "Diabetes": this publication is before the effective filing date of the present application – a copy of the publication is included with this paper for the Office's convenience) describes that "routine diagnosis of type 1 diabetes based on beta cell-specific auto-antibodies was being implemented before [the effective filing date of the present application]."

In summary, Type 1 diabetes is an autoimmune disease resulting from specific destruction of the insulin-producing beta cells of the Langerhans islets of the pancreas. It has been demonstrated that the physiological destruction of beta cells is a crucial event at disease outset, initiating autoimmunity against these cells. Autoantibodies to beta cells are detectable long before a person develops diabetes. Discrimination between Type 1 and Type 2 diabetes is important for determining the most appropriate treatment, and this can be performed by detecting auto antibodies targeting beta cells of the islets of Langerhans. Routine diagnosis of Type 1 diabetes based on beta cell-specific auto-antibodies was being implemented before the effective filing date of the present application. As described in the present specification, ZnT-8 is a beta-cell specific protein. Auto antibodies are described in the present specification. Thus, based on what was known at effective filing date of the present specification, one of ordinary skill in the art would readily recognize that auto antibodies

directed against ZnT-8, a beta-cell specific antigen, could be used as markers for the prognosis and diagnosis of Type 1 diabetes, and the skilled artisan, reading the present specification, would immediately find it useful to detect anti-ZnT-8 auto antibodies because of their use as a diagnostic tool and prognosis marker. Accordingly, Applicants submit that present Claim 39, drawn to "A method detecting Type 1 diabetes by detecting the presence of auto antibodies specifically targeting the beta cells of the pancreatic islets of Langerhans" has utility.

Withdrawal of the 35 U.S.C. Section 101 rejection is respectfully requested.

The enablement rejection of Claims 39-46 is respectfully traversed. Applicants note that present Claim 39 is drawn to "A method detecting Type 1 diabetes by detecting the presence of auto antibodies specifically targeting the beta cells of the pancreatic islets of Langerhans ..."

At the outset, the Office has asserted at page 7 of the Official Action that "In Example, 3, only $\beta$ cells were probed for ZnT-8 mRNA expression." Thus, the Office has admitted, on the Record, that the specification describes ZnT-8mRNA expression in $\beta$ cells. Further, while the Office has asserted that "even the data that are provided cannot be interpreted as the figures are essentially illegible," the Office, in the Official Action, has not objected to these figures. Absent a formal objection to the figures, Applicants must conclude the figures are legible and the Office is incorrect in relying on an "illegible" argument. Finally, Applicants note that the standard for enablement is being able to make and use the invention without undue experimentation. The standard does not preclude experimentation, only undue experimentation. As described above, routine diagnosis of Type 1 diabetes based on beta cell-specific auto-antibodies was being implemented before the effective filing date of the present application; and ZnT-8 is a beta-cell specific protein. Auto antibodies are

described in the present specification. Thus, based on what was known at effective filing date of the present specification, one of ordinary skill in the art would readily recognize that auto antibodies directed against ZnT-8, a beta-cell specific antigen, could be used as markers for the prognosis and diagnosis of Type 1 diabetes, and that the technique of detecting auto antibodies were readily available. Accordingly, given this knowledge, Applicants submit that one of ordinary skill in the art, with some, but not undue, experimentation, could make and use the invention as claimed. Withdrawal of the rejection is respectfully requested.

The written description rejection of Claims 39-46 is respectfully traversed. Paragraph 34 of the originally filed specification describes "diabetes diagnosis." Paragraph 35 of the originally filed specification describes "....a subject of the present invention is the use, as a specific marker for the beta cells of pancreatic islets of Langerhans, of at least one isolated polynucleotide or of the corresponding protein." At originally filed Claim 29, that is part of the originally filed specification, the term "auto antibodies" is described (e.g., "the search for auto antibodies directed against said protein."). Paragraph 104 of the originally filed specification, describes, in part "...the search for auto-antibodies directed against the protein according to the invention." Paragraph 2 of the originally filed specification describes "Type 1 diabetes." Taking all of these descriptions together, Applicants submit that present Claim 39, drawn to "A method detecting Type 1 diabetes by detecting the presence of auto antibodies specifically targeting the beta cells of the pancreatic islets of Langerhans ..." is described in the originally filed specification. Withdrawal of the rejection is requested.

The rejection of Claims 39-46 under 35 U.S.C. 112, second paragraph, for omitting essential steps, is believed to be obviated by the amendment of Claim 39. Withdrawal of the rejection is respectfully requested.

Because Applicants believe the present application is now in condition for allowance, Applicants request rejoinder of the withdrawn claims.

Applicants submit the present application is now in condition for allowance. Early notification to this effect is earnestly solicited.

Respectfully submitted,

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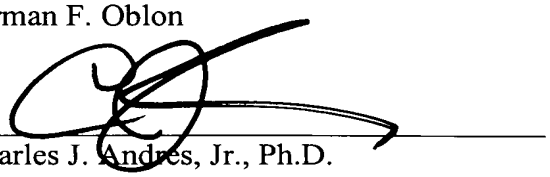

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